Bisphenol A Substitutes: Are They Safe?

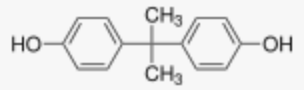
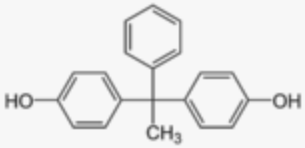
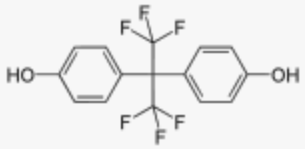
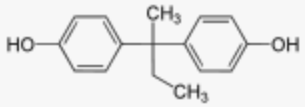
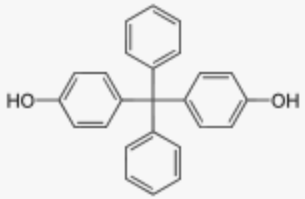
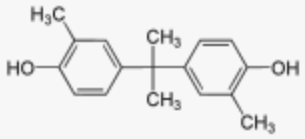
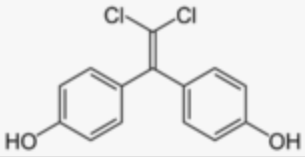
Johanna R. Rochester

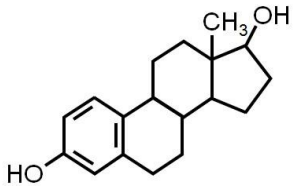
March 18th 2015

TEDX
The Endocrine Disruption Exchange

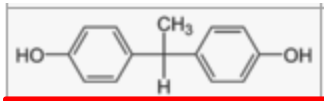
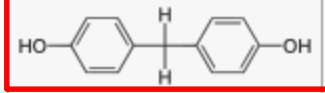
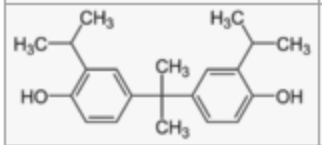
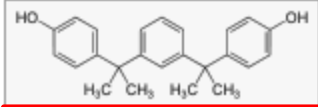
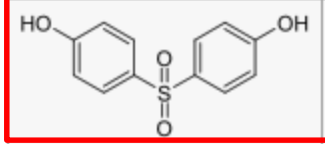
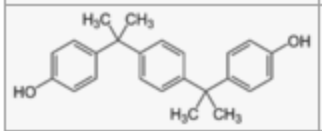
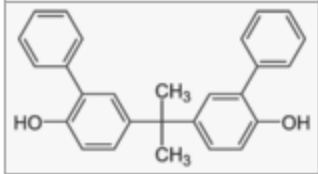
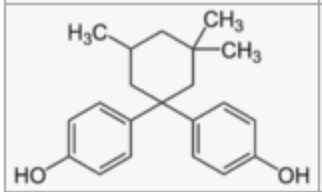
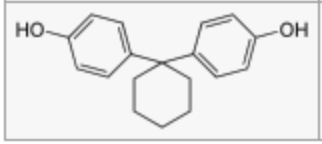
BPA Substitutes

- BPA is an endocrine disrupting chemical (EDC)
- Growing consumer concern has prompted use of alternatives to BPA by manufacturers
- Many are bisphenol analogues
- Can be in products labeled “BPA free”

Structural formula	Name	CAS
	Bisphenol A	80-05-7
	Bisphenol AP	1571-75-1
	Bisphenol AF	1478-61-1
	Bisphenol B	77-40-7
	Bisphenol BP	1844-01-5
	Bisphenol C	79-97-0
	Bisphenol C	14868-03-2



17β-estradiol (E2)
natural estrogen

	Bisphenol E	
	Bisphenol F	87139-40-0
	Bisphenol G	127-54-8
	Bisphenol M	13595-25-0
	Bisphenol S	80-09-1
	Bisphenol P	2167-51-3
	Bisphenol PH	24038-68-4
	Bisphenol TMC	129188-99-4
	Bisphenol Z	843-55-0

Bisphenol S and F: A Systematic Review and Comparison of the Hormonal Activity of Bisphenol A Substitutes

Johanna R. Rochester and Ashley L. Bolden
Environmental Health Perspectives
Published online March 16th 2015

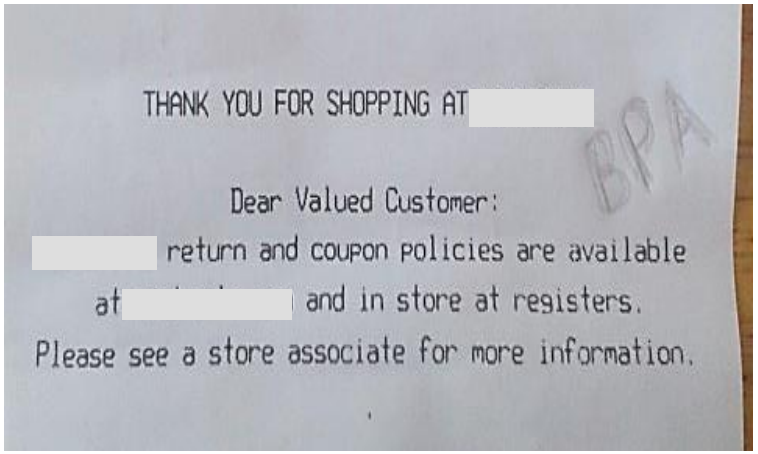
- Systematic Review
  - Focused on a research question
  - Comprehensive, structured, transparent
  - Study quality
  - Data synthesis

Overview

- Bisphenol A (BPA) as an endocrine disrupting chemical (EDC)
- BPA substitutes: BPS and BPF hormonal activity
- Potency of BPS and BPF compared to BPA
- Conclusions/Recommendations

Bisphenol A

- Known estrogen since the 1930s
- Modern Uses
  - Hard plastic
    - Recycling codes #7, #3
  - Thermal receipt paper
  - Dental sealants/fillings
  - Can linings



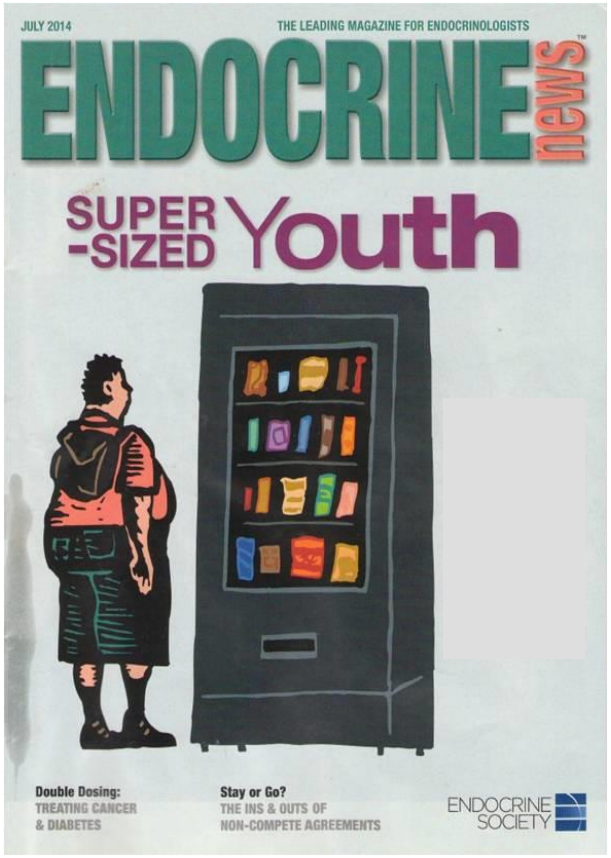
- >3.5 million tonnes produced per year
- Humans exposed through diet, skin, dust

BPA as an EDC

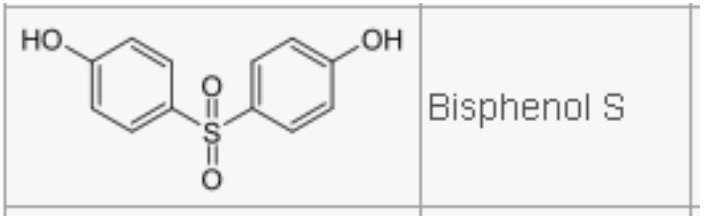
- Hundreds of studies
- *In vitro* and *in vivo*
  - Binds to estrogen, androgen, thyroid receptors
  - Disrupts reproduction, central nervous system, endocrine pancreas, immune system

BPA and Human Health

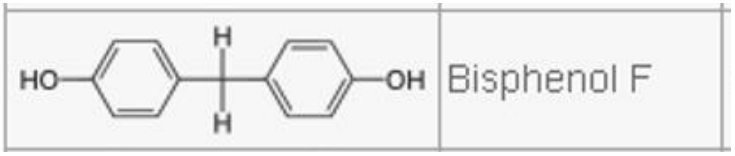
- Over 75 epidemiological studies Rochester 2013. URL: http://www.ncbi.nlm.nih.gov/pubmed/23994667
- Disrupted reproduction, development, metabolic system, thyroid system, immune system, etc.
- Adulthood
- Development



BPA Substitutes

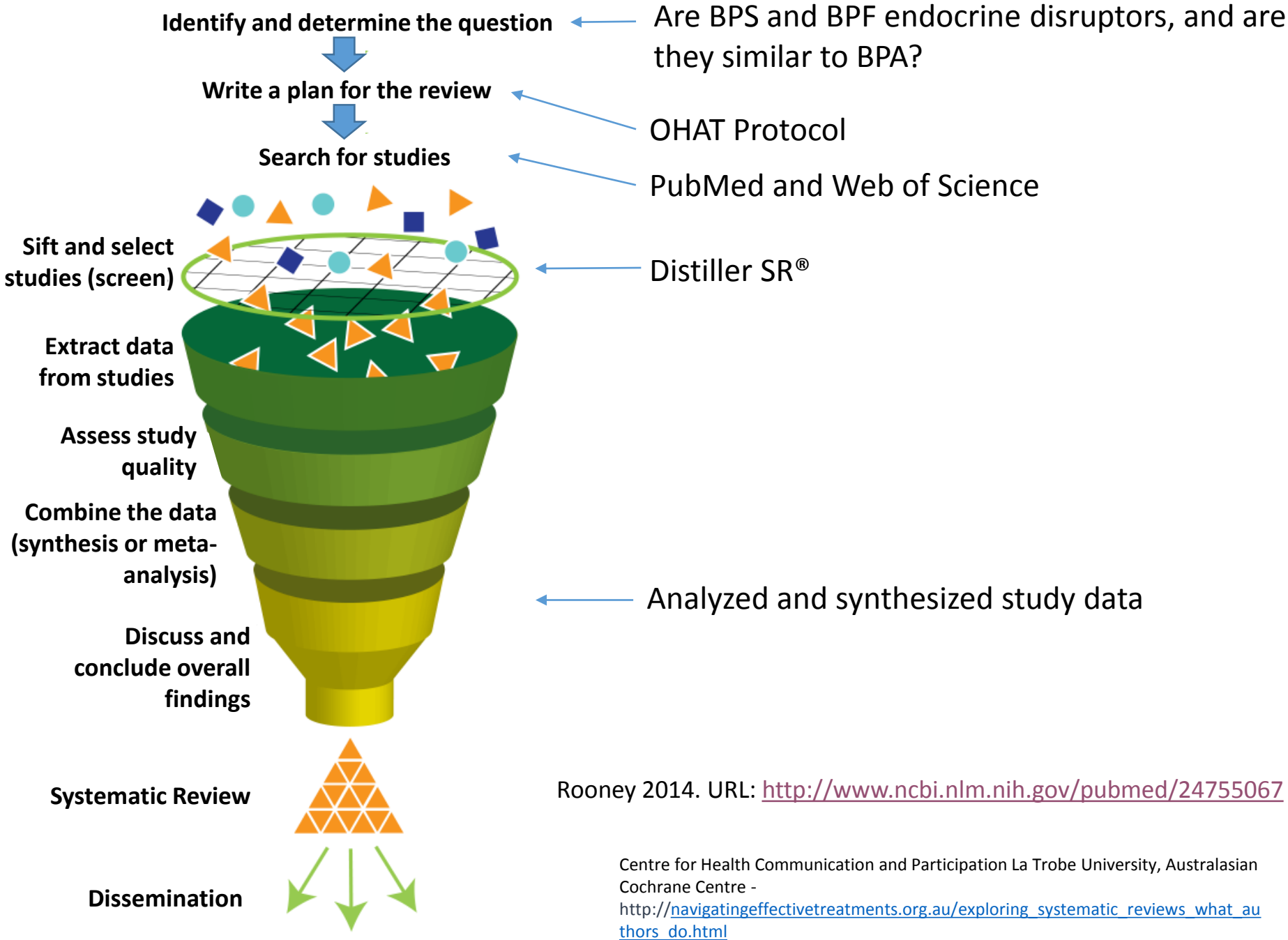


- BPS
  - Industrial uses
  - Thermal reciept paper (“BPA-free”)



- BPF
  - Industrial uses
  - Consumer uses
- Found in personal care products, paper products, food, dust, water, sewage effluent
- Both found in human urine at concentrations comparable to BPA

Liao 2012. URL: http://www.ncbi.nlm.nih.gov/pubmed/22620267
Zhou 2014. URL: http://www.ncbi.nlm.nih.gov/pubmed/24316527



Are BPS and BPF endocrine disruptors, and are they similar to BPA?

OHAT Protocol

PubMed and Web of Science

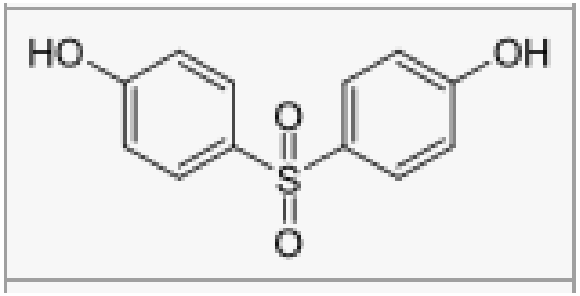
Distiller SR®

Analyzed and synthesized study data

Rooney 2014. URL: http://www.ncbi.nlm.nih.gov/pubmed/24755067

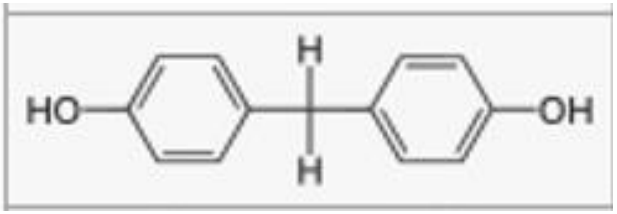
Centre for Health Communication and Participation La Trobe University, Australasian Cochrane Centre - http://navigatingeffectivetreatments.org.au/exploring_systematic_reviews_what_authors_do.html

Results: BPS activity



- *In vitro*:
  - Estrogenic
  - Androgenic
  - Anti-androgenic
  - Enzyme changes (caspase-8), liver cells, serum albumin binding, DNA damage
- *In vivo:*
  - Daphnia—acute toxicity
  - Zebra fish—reduced gonad weight, changes in serum hormones, disrupted reproduction
  - Rats—increased uterine growth

Results: BPF activity

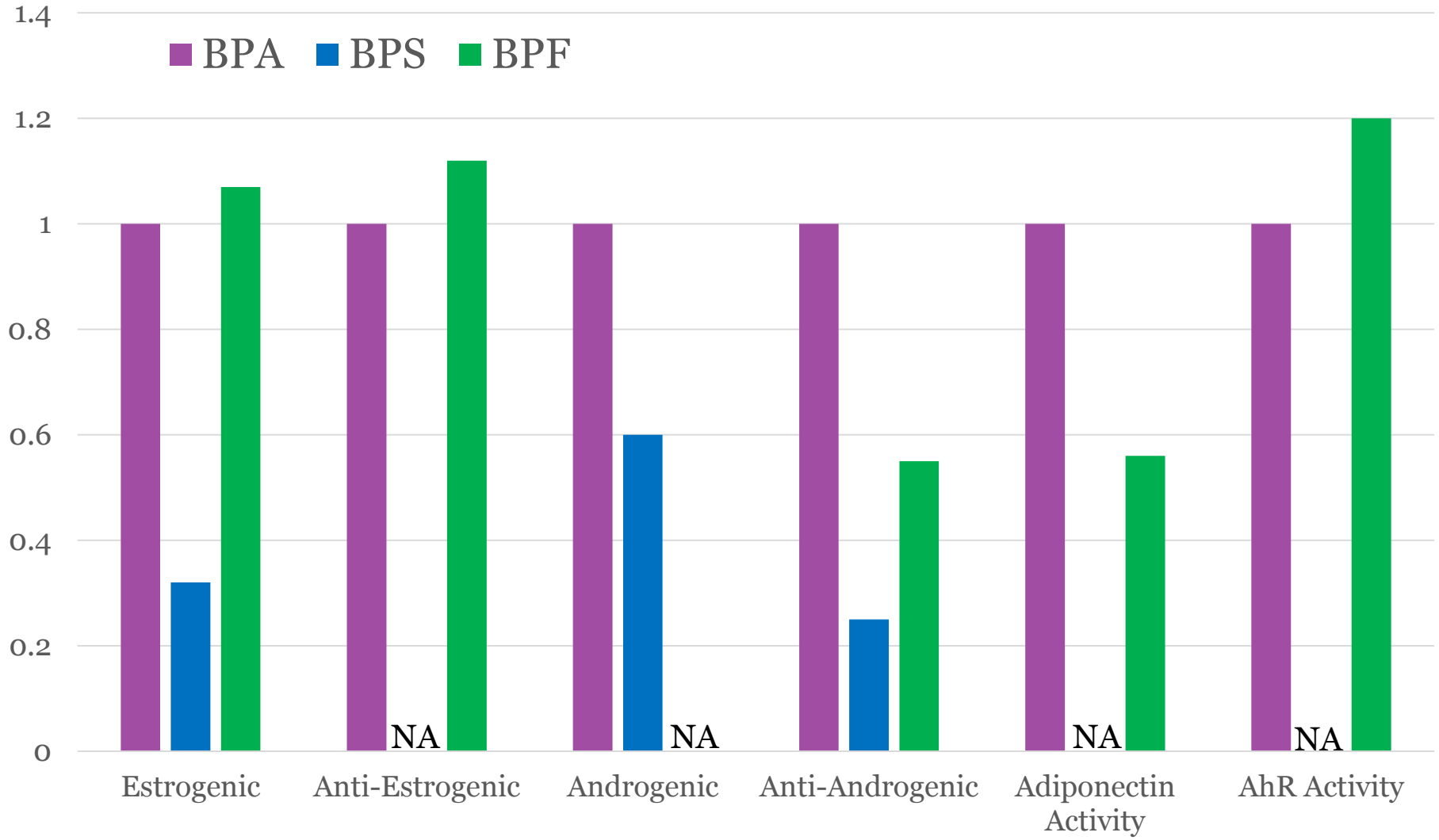


- *In vitro*:
  - Estrogenic
  - Anti-estrogenic
  - Anti-androgenic
  - Cytotoxicity, cellular dysfunction, DNA damage
- *In vivo:*
  - Daphnia—acute toxicity
  - Rats—increased uterine growth, increased male sex organ weight, thyroid disruption

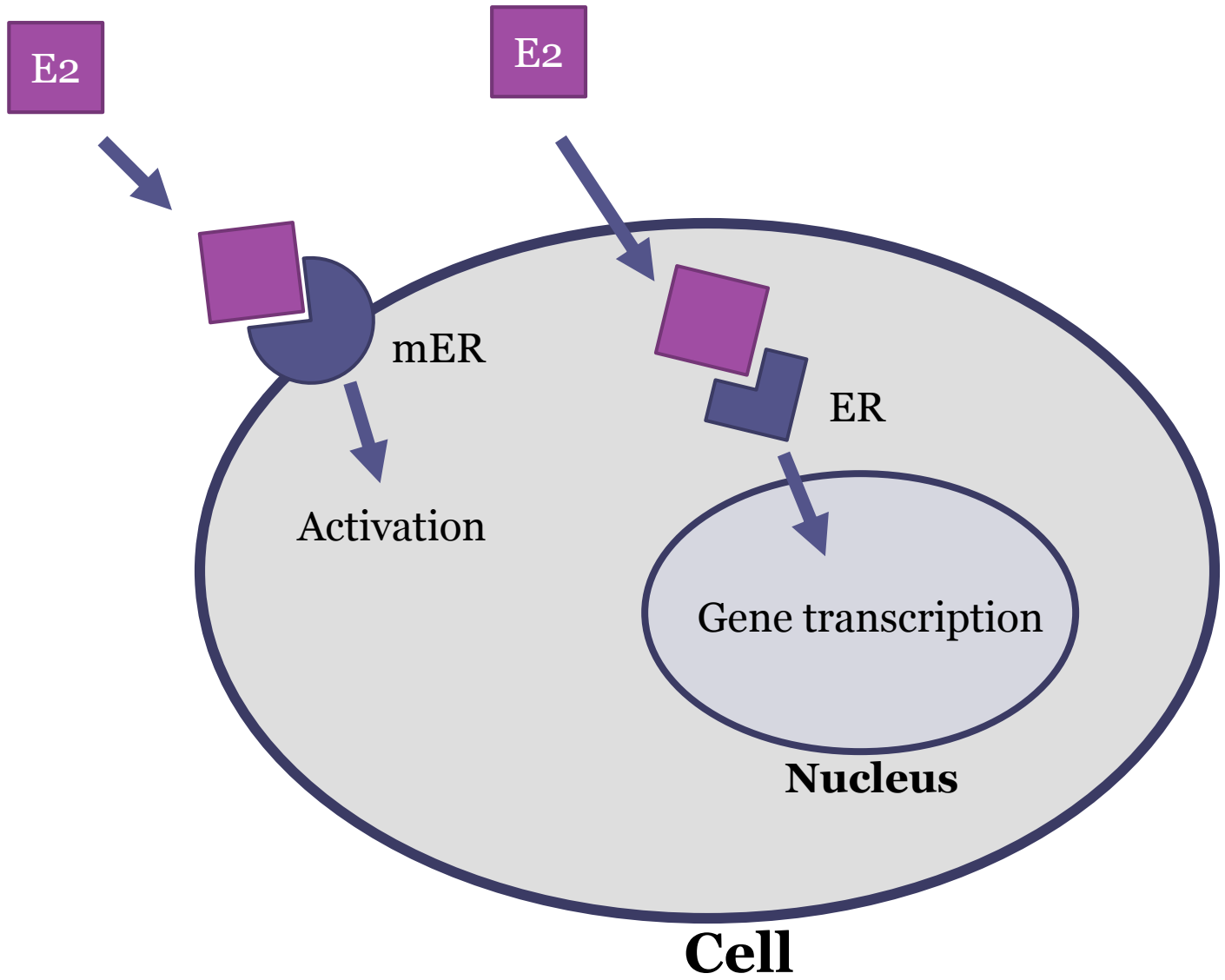
How do BPS/BPF compare to BPA?

- Analyzed studies that tested BPF and/or BPS and BPA in the **same assay**
- *In vitro*
- Relative Potencies were calculated by dividing the BPS or BPF potency by the BPA potency in the same study

Relative Potency of BPS/BPF (Compared to BPA)



Different Pathways of Estrogen Action

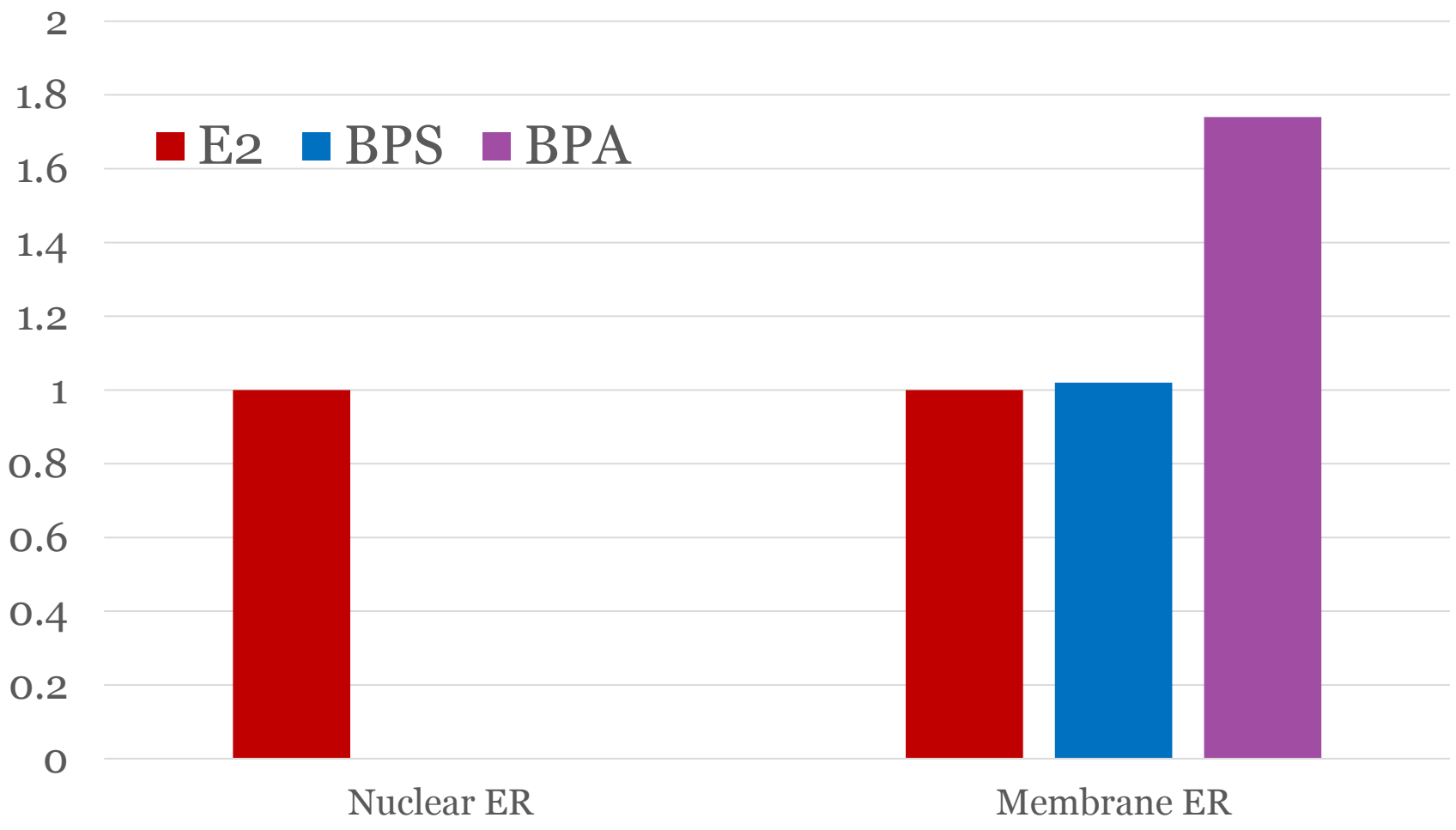


Estrogenic Activity

- BPA, BPS, and BPF are considered "weak" estrogens in *nuclear* receptor models
  - 10^{-6} to 10^{-4} times less potent than E2
- However in *membrane* receptor models, BPA and BPS are of similar and greater potency to E2

Vinas 2013a. URL: http://www.ncbi.nlm.nih.gov/pubmed/23458715
Vinas 2013b. URL: http://www.ncbi.nlm.nih.gov/pubmed/23530988

Relative Potency of BPA/BPS (Compared to Estradiol (E2))



Conclusions

- BPS and BPF are EDCs
- Similarly potent to BPA via many hormonal activities and actions
- BPS and BPF are not good substitutes for BPA

Recommendations

- Chemicals should be tested before being released
  - "Regrettable Substitutes"
- Classes of chemicals should be regulated
- Research should be directed towards developing biologically inert substitutes for harmful chemicals

Acknowledgements

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- TEDX Team: Carol Kwiatkowski, Lynn Carroll, Chris Ribbens, Kim Schultz

- This manuscript was dedicated to Dr. Theo Colborn (1927-2014), founder of TEDX